
Control Groups vs Comparison Groups

Overview

- Control conditions
- Behavioral placebos
- Conclusions

Control Conditions

- Historical control
- Waiting list controls

Control Conditions

- Standard care control
- Comparison condition control
- Behavioral placebo condition

Placebo Quiz

- 1. Usually 33% of patients will respond to placebo
- 2. Placebo effects are short-lived
- 3. Placebo effects play more of a role in behavioral studies than in drug studies
- 4. Placebo responders=subgroup
- 5. Placebo effects are influenced by past treatment

Definition and Background

Definition

- “A placebo is an intervention designed to simulate a behavioral intervention but not believed (by the investigator) to be a specific therapy for the target condition”
 - » Turner, J., Deyo, R., Loeser, J. Von Korff, M., & Fordyce, W. JAMA, 1994, 1609-1614.

Definition: Key Points

- Simulates intervention
- Placebo is not believed to be specific for target condition

Placebo Simulates Intervention

- Non-specific effects
- Therapist attention, interest, and concern
- Patient and therapist expectations
- Reputation, expensiveness, and impressiveness of treatment
- Characteristics of setting

Effects of Placebos

The Powerful Placebo

- Beecher (1955)
- 15 studies of pain, $N > 1,000$
- “Placebos have a high degree of therapeutic effectiveness...being produced in $35.2 \pm 2.2\%$ of patients”

Medical Placebo Effects

- Sham medical treatments are effective—e.g. sham toothgrinding reduces TMD pain in 64% of patients
- Treatments initially considered effective but later shown no better than placebo show high rate of success
- Medical placebos produce side effects and carryover effects that mimic medication

Surgical Placebo: 1950s

- 1950s: Two double-blind randomized trials of internal mammary artery ligation vs skin incision (placebo) for angina pectoris
- Both studies showed substantial and sustained improvements after skin incision alone

Surgical Placebo 2002

- Mosely, O'Malley, Peterson, Brody, et al. (NEJM, 2002, 347, 81-88)
- Does arthroscopic surgery work for OA?
- N=180 VA patient
- 1. Arthroscopic debridement
- 2. Arthroscopic lavage
- 3. Placebo surgery
- Evaluations: pre, post, 24 mos.
- Knee pain rating, functional assessments, SF 36

Placebo Surgery

- Simulated arthroscopic debridement
- Knee prepped and draped
- 3, 1 cm incisions made in skin
- Surgeon asks for all instruments, manipulated knee as if arthroscopy
- Patient in OR for same time period

Moseley, et al. (2002)

- Compared to placebo surgery, neither intervention group reported less pain or better function at any time point
- Efficacy of surgery is no better than placebo

Placebo Meta Analysis

- Hrobjartsson & Gotzsche (2001)
- 32 binary outcome trials, 82 continuous outcome trials
- Placebo had no effect on binary outcomes
- Placebo had modest effect in small trials
- Placebo significant effect in pain trials (6.5 mm on 100 mm VAS)

Behavioral Placebos

Basic Elements of a Behavioral Placebo

- 1.
- 2.
- 3.
- 4.
- 5.
- 6.

Behavioral Placebo to test CBT

- Blanchard et al. (1992) combined:
- Pseudomeditation=mental scan of muscles (but don't relax muscles) plus imagery of daily activities
- Alpha EEG suppression=auditory feedback of alpha EEG plus verbal encouragement

Key Findings

- Credibility high (mean=7.9 vs mean=8.5 for treatment group)
- High level of practice (mean=7.7 practices per week vs mean=6.9 tx)
- Performance=placebo showed “average” (9.1%) decreases in level of EEG over sessions
- Success rated by patient=6.5 on 9 point scale

Outcome

- CBT as effective as placebo: Why?
- Patients reported using the pseudomeditation to relax and calm themselves, despite being told not to relax

Supporting Findings

- Placebo group:
- Finger temp. increased within and across sessions
- Showed significantly higher reported use of “mental imagery”
- Placebo treatment was not neutral

Behavioral Placebo: Challenges

- 1. Behavioral placebos are not psychologically inert
- 2. Behavioral placebos often not credible to patients or therapists
- 3. Impossible to keep therapists blind
- 4. Conducting a behavioral placebo over long time periods is difficult for therapists ethically
- 5. Studies with behavioral placebos often fail to test specific, key components of “treatment packages”

Discussion

Mechanisms of Placebo

- 1. Personality traits of patient
- 2. Interpersonal/contextual variables
- 3. Expectancy/meaning
- 4. Classical conditioning
- 5. Biological mechanisms
 - » Endorphins
 - » Neuroendocrine

Biological Mechanisms

- Leuchter, Cooke, Witte, et al. (Am. J. Psychiatry, 2002,159: 122-129)
- Question: Can quantitative EEG (QEEG) detect differences in brain function between medication and placebo responders?

Study Design

- N=51 Ss major depression
- All Ss had been in one of two 9 week, placebo controlled trials testing efficacy of fluoxetine or venlafaxine
- Serial QEEG recordings performed (baseline, 2 days, 1-, 2-, 4-, and 8-weeks)
- Subjects classified as medication responders/non-responders, placebo responders/non-responders

QEEG

- Regional quantitative EEG (relative power in four frequency bands: 0.5-4Hz, 4-8Hz, 8-12 Hz, and 12-20 Hz)
 - » Prefrontal
 - » Central
 - » Temporal
 - » Parietal
 - » Occipital
- Cordance
 - » Associated with cerebral perfusion (PET)
 - » Normalizes power across bands and electrode sites

Results

- No pre-tx differences among four outcome groups
- Placebo responders showed a significant increase in prefrontal cordance early in treatment not shown in medication responders (who showed a decrease) or other groups

Conclusions

- “Effective” placebo treatment induces changes in brain function that are distinct from those associated with antidepressant medication
- Administration of an “inert” placebo=active treatment
- Placebo response is not functionally the same as medication response
- Placebo and active medication may have distinct mechanisms of action

Placebo Research Agenda: Guess, Kleinman, Kusek, & Engel (2002)

● Science

1. Identify moderators
2. Examine biological mechanisms
3. Develop new tools
4. Refine theories to integrate bio-, psycho-, social variables

● Clinical Applications

1. How optimize placebo effects?
2. Can placebo be self-induced?
3. Pt-provider dynamics
4. Identify barriers to placebo

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